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EXAMINER	
HUTZELL, P	

ART UNIT	PAPER NUMBER
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DATE MAILED: 09/19/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 5/10/95 & 5/19/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1 - 19 are pending in the application.
   Of the above, claims 6 and 9-13 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-5, 7, 8 and 14-19 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. If applicant desires priority under 35 U.S.C. § 120 based upon a parent application, specific reference to the parent application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. Status of the parent application (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "Patent No." should follow the filing date of the parent application. If a parent application has become abandoned, the expression "abandoned" should follow the filing date of the parent application.

16. Applicant's election without traverse of Group I, claims 1-5, 7-8 and 14-19 in Paper No. 7 is acknowledged. Upon further consideration and search, Group II has been rejoined with Group I for examination. Accordingly, claims 1-8 and 14-19 are under consideration. Claims 9-13 are withdrawn from consideration as being drawn to non-elected inventions.

17. Claims 1-5, 7 and 8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,202,253. Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The antibody claimed herein is has the identical properties and variable region amino acid sequences as the HPC-4 monoclonal antibody claimed in U. S. Patent No. 5,202,253. The limitation in instant claim 1, that the subject antibody is recombinant is given no weight in comparing the claims with those of the '253 patent, since this limitation is deemed to confer no structural difference between the claimed antibody and the prior art antibody.

18. Claims 14-19 are rejected under the judicially created

doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,202,253 in view of Morrison or Queen.

It would have been obvious to use immunoglobulin gene cloning methods such as those described by Morrison in order to clone the genes encoding the antibody claimed in claims 1-3 of U.S. Patent No. 5,202,253.

19. Claim 6 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,202,253 in view of U.S. Patent No. 5,147,638.

It would have been obvious to combine an antibody as claimed in U.S. Patent No. 5,202,253, which has a variable region identical to the antibodies claimed herein, with a cytokine in view of the suggestion in col. 5 of the '638 patent that anti-protein C antibodies in combination with cytokines would be useful for treatment of tumors.

20. The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. *In re Vogel*, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

22. Claims 1, 2, 4, 5, 7 and 8 are rejected under 35 U.S.C. § 102(b) and (e) as being anticipated by U.S. Patent No. 5,202,253 or U.S. Patent No. 5,147,638.

Each of U.S. Patent No. 5,202,253 and U.S. Patent No. 5,147,638 teach monoclonal antibody HPC-4, which inherently possesses the characteristics recited in claims 1-5, 7 and 8. The limitation in claim 1 that the subject antibody is recombinant is given no weight in comparing the claims with the prior art, since this limitation is deemed to confer no structural difference between the claimed antibody and the prior art antibody.

23. Claims 1, 2, 4, 5 and 8 are rejected under 35 U.S.C. § 102(b) as being anticipated by D'Angelo et al. (J. Clin. Invest. 77). Claims 1, 2, 4, 5, 7 and 8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Stearns et al. (J. Biol. Chem. 263).

Each of D'Angelo et al. and Stearns et al. teach monoclonal antibody HPC-4. The references teach monoclonal antibody HPC-4 coupled to Affigel 10 and coupled to immunobeads (pages 417 and

827, respectively). Stearns additionally teach monoclonal antibody HPC-4 bound to metal ions such as Tb^{+3} and Ca^{2+} which is considered to meet the limitations of claim 6, given that binding of the HPC-4 antibody to metal ions increased the intrinsic protein fluorescence which was detected in fluorescence assays.

24. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

25. Claims 1-8 and 14-19 are rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent No. 5,202,253 or U.S. Patent No. 5,147,638 or D'Angelo et al. (J. Clin. Invest. 77) or Stearns et al. (J. Biol. Chem. 263) in view of Morrison or Queen.

U.S. Patent No. 5,202,253, U.S. Patent No. 5,147,638, D'Angelo et al. (J. Clin. Invest. 77) and Stearns et al. (J. Biol. Chem. 263) teach monoclonal antibody HPC-4, as previously discussed.

Morrison and Queen teach that methods for immunoglobulin gene cloning and expression were well established in the art at the time

the claimed invention was made.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the basic methods taught by Morrison or Queen in order to clone the genes encoding the HPC-4 monoclonal antibody taught by U.S. Patent No. 5,202,253 or U.S. Patent No. 5,147,638, D'Angelo et al. (J. Clin. Invest. 77) and Stearns et al. (J. Biol. Chem. 263). In doing so one of ordinary skill in the art would have obtained antibodies and DNAs encoding antibodies having the structural characteristics of those claimed. One of ordinary skill in the art would have been motivated to produce recombinant antibodies having the variable region of HPC-4 in order to obtain the advantages discussed by Morrison, for example, on page 1207. One would have been motivated to produce chimeric antibodies or humanized antibodies comprising human antibody sequences in view of the art-recognized advantages of reduced immunogenicity in human hosts obtained by replacing rodent antibody sequences with human sequences as discussed by Morrison and Queen. It would have been obvious to formulate compositions comprised of recombinant HPC-4 and a cytokine or an inducer of cytokine expression in view of the teaching of U.S. Patent No. 5,147,638 in column 5, that anti-protein C antibodies in combination with cytokines were considered to be useful for treatment of tumors.

26. Claims 2, 4, 15 and 16 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims

limited to antibodies having the functional properties recited in claim 1 wherein the antibodies are characterized as having the heavy chain depicted in Seq ID NO. 10 paired with the light chain depicted in SEQ ID NO. 12, or said sequences minus the signal sequences. It is unpredictable that antibodies comprising only the individual heavy or light chains of the HPC-4 antibody or the heavy and light chains of HPC-4 paired with variable region polypeptides from different antibodies, as encompassed by the claim will be capable of binding to the activation peptide of protein c in combination with calcium and inhibiting protein C activation by thrombin-thrombomodulin. It is generally accepted by those of skill in the art that properly associated heavy and light chain variable regions are required in order to obtain antigen binding function, in the absence of evidence to the contrary. The record contains no evidence which would allow one of skill in the art to predict that the 4 polypeptides recited in claim 2 individually possess the functions recited in claim 1. It appears that undue experimentation would be required to practice the invention as claimed in claim 2. Similar criticisms apply to claims 4, 15 and 16. See M.P.E.P. §§ 706.03(n) and 706.03(z).

27. Claims 3 and 16 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention.

Claims 3 and 16 are indefinite in the recitation of an antibody containing "human amino acid sequence" and "human sequence", respectively. The nature of the human sequence, e.g. a human framework, constant region, CDR region, a single amino acid is not known. Thus, the defining structural characteristics of the antibody and method defined by the claims are not known. The specification describes only humanized antibodies which are comprised of CDRs of non-human origin and all other regions of human origin.

28. Claims 1-8 and 14-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation of an antibody which binds to the peptide defined by Seq. ID No. 1 in combination with calcium because the intended meaning is unclear. It is unclear whether the subject antibody binds to an epitope which includes calcium or whether calcium binds to a site on the antibody not involved in epitope recognition. Claims 5 and 6 are confusing in the respective recitations of an antibody comprising a carrier and an antibody comprising a cytokine or an inducer of cytokine expression. It appears that the claims should be drawn to compositions comprising an antibody and the specified additional ingredients. Claim 8 is confusing in the recitation of an antibody

immobilized to a substrate wherein the immobilized antibody is suitable for purification of protein C. It is unclear whether the intended meaning is that substrate to which the antibody is immobilized is one which is suitable for the production of an affinity matrix or whether the suitability of the antibody for purification resides in the inherent properties of the antibody irrespective of the nature of the substrate to which it is bound. Insertion of indefinite articles prior to "amino acid" in claims 2 and 15.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Paula Hutzell, Ph.D, whose telephone number is (703) 308-4310. The Examiner can normally be reached on Monday-Thursday from 9:00 AM-6:00 PM. The Examiner can also be reached on alternate Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Margaret Parr, can be reached on (703)-308-2454. The fax phone number for this Group is (703)-305-7401.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

PAULA K. HUTZELL
PRIMARY EXAMINER
GROUP 1800